

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Paz Einat, et al.
U.S. Serial No. : 10/561,005
Filed : as §371 national stage of PCT
International Application No.
PCT/IL2004/000515
For : METHODS FOR CLONING NUCLEIC ACIDS IN
A DESIRED ORIENTATION

1185 Avenue of the Americas
New York, New York 10036
May 24, 2006

Mail Stop PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**AMENDMENT IN RESPONSE TO MARCH 24, 2006 NOTIFICATION TO COMPLY
WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

This Amendment is submitted in response to the March 24, 2006 Notification to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures issued by the United States Patent and Trademark Office in connection with the above-identified application. The March 24, 2006 Notification, a copy of which is attached hereto as **Exhibit A**, provides two (2) months for filing a response. Therefore, a response to the March 24, 2006 Notification is due May 24, 2006. Accordingly, this Amendment is being timely filed.

Amendments to the Specification begin on page 2 of this paper.

A substitute **Sequence Listing** is referred to on page 6 of this paper and attached hereto as **Exhibit B**.

Remarks begin on page 7 of this paper.

JAW

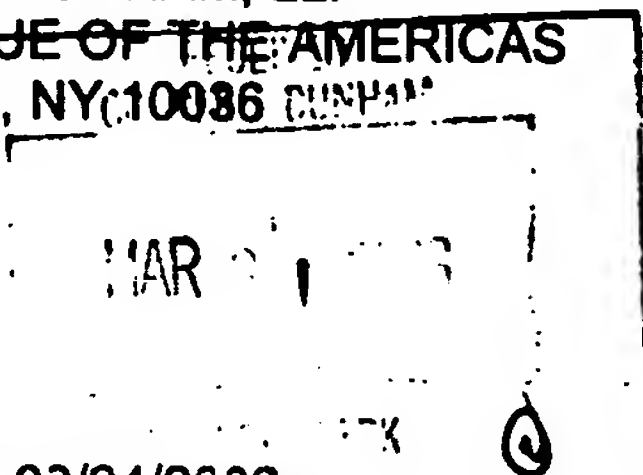


UNITED STATES PATENT AND TRADEMARK OFFICE

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U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
10/561,005	Paz Einat	69626-A-PCT-US/JPW/JW

23432
COOPER & DUNHAM, LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036



Date Mailed: 03/24/2006

2mo - 5/24/06
3mo - 6/24/06
4mo - 7/24/06
5mo - 8/24/06
6mo - 9/24/06
7mo - 10/24/06

INTERNATIONAL APPLICATION NO.	
PCT/IL04/00515	
I.A. FILING DATE	PRIORITY DATE
06/15/2004	06/16/2003

CONFIRMATION NO. 9425
371 FORMALITIES LETTER
OC000000018367668

**NOTIFICATION TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS
CONTAINING NUCLEOTIDE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Applicant is given **TWO MONTHS FROM THE DATE OF THIS NOTICE** within which to file the items indicated below to avoid abandonment. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing." Applicant must provide a substitute computer readable form (CRF) copy of the "Sequence Listing" and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d).

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

For questions regarding compliance to 37 CFR 1.821-1.825 requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For Patent Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.
- Send e-mail correspondence for Patent Software Program Help @ ebc@uspto.gov

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

*A copy of this notice **MUST** be returned with the response.*

DEBORAH D WILLIAMS

Telephone: (703) 308-9140 EXT 205

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PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/561,005	PCT/IL04/00515	69626-A-PCT-US/JPW/JW

FORM PCT/DO/EO/922 (371 Formalities Notice)

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Biotechnology Systems Branch

RAW SEQUENCE LISTING

ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number:

10/561,005

Source:

IFWP

Date Processed by STIC:

12/30/05

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 4.2.2 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail. Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom. Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 11/14/05): U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/24/05

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- 1 **Wrapped Nucleic Acid** The number text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved from word processor after creating it. Please adjust your margins to 3" this will prevent wrapping.
- 2 **Invalid Line Length** The rules require that a line not exceed 72 characters in length. This includes white spaces.
- 3 **Misaligned Amino Numbering** The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
- 4 **Non-ASCII** The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
- 5 **Variable Length** Sequence(s) contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
- 6 **PatentIn 2.0 "bug"** A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s). Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.
- 7 **Skipped Sequences (OLD RULES)** Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence:
(2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
(i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
This sequence is intentionally skipped
Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.
- 8 **Skipped Sequences (NEW RULES)** Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence:
<210> sequence id number
<400> sequence id number
000
- 9 **Use of n's or Xaa's (NEW RULES)** Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.
- 10 **Invalid <213> Response** Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence
- 11 **Use of <220>** Sequence(s) missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.
(See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
- 12 **PatentIn 2.0 "bug"** Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
- 13 **Misuse of n/Xaa** "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid

RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/561,005

DATE: 12/30/2005

TIME: 09:45:20

Input Set : A:\103-PCT1-US1-ST25.txt

Output Set: N:\CRF4\12302005\J561005.raw

3 <110> APPLICANT: Paz Binat et al./Quark Biotech, Inc.

5 <120> TITLE OF INVENTION: Methods for cloning nucleic acids in a desired orientation

7 <130> FILE REFERENCE: 103/PCT1-US1

9 <140> CURRENT APPLICATION NUMBER: US/10/561,005

10 <141> CURRENT FILING DATE: 2005-12-16

12 <150> PRIOR APPLICATION NUMBER: PCT/IL 2004/000515

13 <151> PRIOR FILING DATE: 2004-06-15

15 <150> PRIOR APPLICATION NUMBER: 60/479,224

16 <151> PRIOR FILING DATE: 2003-06-16

18 <160> NUMBER OF SEQ ID NOS: 14

20 <170> SOFTWARE: PatentIn version 3.2

22 <210> SEQ ID NO: 1

23 <211> LENGTH: 24

24 <212> TYPE: DNA

25 <213> ORGANISM: Artificial

27 <220> FEATURE:

28 <223> OTHER INFORMATION: Artificial DNA

31 <220> FEATURE:

32 <221> NAME/KEY: misc_feature

33 <222> LOCATION: (21)..(24)

34 <223> OTHER INFORMATION: "n"=nucleotide A, T, G or C

36 <400> SEQUENCE: 1

OK 37 gccattaagg ccaccatgcc nnnn

40 <210> SEQ ID NO: 2

41 <211> LENGTH: 41

42 <212> TYPE: DNA

43 <213> ORGANISM: Artificial

45 <220> FEATURE:

46 <223> OTHER INFORMATION: Artificial DNA

48 <400> SEQUENCE: 2

49 catggtggcc ttaatggcca ctacgaccgt tcgggtggta c

52 <210> SEQ ID NO: 3

53 <211> LENGTH: 24

54 <212> TYPE: DNA

55 <213> ORGANISM: Artificial

57 <220> FEATURE:

58 <223> OTHER INFORMATION: Artificial DNA

61 <220> FEATURE:

62 <221> NAME/KEY: misc_feature

63 <222> LOCATION: (21)..(24)

64 <223> OTHER INFORMATION: n=nucleotide A, T, G or C

66 <400> SEQUENCE: 3

OK 67 gccattaagg ccaccatgcc nnnn

Does Not Comply
Corrected Diskette Neededinsufficient explanation
(give source of genetic material)
(see item 11 on Error
summary
sheet)

24

41

24

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70 <210> SEQ ID NO: 4
71 <211> LENGTH: 41
72 <212> TYPE: DNA
73 <213> ORGANISM: Artificial
75 <220> FEATURE:
76 <223> OTHER INFORMATION: Artificial DNA
78 <400> SEQUENCE: 4
79 catggtgggc ttgocagcat caccggtaat tccggtggta c
82 <210> SEQ ID NO: 5
83 <211> LENGTH: 21
84 <212> TYPE: DNA
85 <213> ORGANISM: Artificial
87 <220> FEATURE:
88 <223> OTHER INFORMATION: Artificial DNA
91 <220> FEATURE:
92 <221> NAME/KEY: misc_feature
93 <222> LOCATION: (1)..(4)
94 <223> OTHER INFORMATION: n = nucleotide A, T, G or C
96 <400> SEQUENCE: 5
97 nnnnggtgag tgactgagga c
100 <210> SEQ ID NO: 6
101 <211> LENGTH: 44
102 <212> TYPE: DNA
103 <213> ORGANISM: Artificial
105 <220> FEATURE:
106 <223> OTHER INFORMATION: Artificial DNA
108 <400> SEQUENCE: 6
109 cgaggagcga ccgactcgat ggccgaggcg gcctcagtc a ctca
112 <210> SEQ ID NO: 7
113 <211> LENGTH: 21
114 <212> TYPE: DNA
115 <213> ORGANISM: Artificial
117 <220> FEATURE:
118 <223> OTHER INFORMATION: Artificial DNA
121 <220> FEATURE:
122 <221> NAME/KEY: misc_feature
123 <222> LOCATION: (1)..(4)
124 <223> OTHER INFORMATION: n = nucleotide A, T, G or C
126 <400> SEQUENCE: 7
127 nnnnggtgag tgactgagga c
130 <210> SEQ ID NO: 8
131 <211> LENGTH: 44
132 <212> TYPE: DNA
133 <213> ORGANISM: Artificial
135 <220> FEATURE:
136 <223> OTHER INFORMATION: Artificial DNA
138 <400> SEQUENCE: 8
139 actcactgac tccggcggag ccggtagctc agccagcgag gaggc
142 <210> SEQ ID NO: 9

41

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44

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143 <211> LENGTH: 13
144 <212> TYPE: DNA
145 <213> ORGANISM: Artificial
147 <220> FEATURE:
148 <223> OTHER INFORMATION: Artificial DNA
150 <400> SEQUENCE: 9
151 gtaccacccgtaacggcgta.g
154 <210> SEQ ID NO: 10
155 <211> LENGTH: 13
156 <212> TYPE: DNA
157 <213> ORGANISM: Artificial
159 <220> FEATURE:
160 <223> OTHER INFORMATION: Artificial DNA
163 <220> FEATURE:
164 <221> NAME/KEY: misc_feature
165 <222> LOCATION: (5)..(9)
166 <223> OTHER INFORMATION: n = nucleotide A, T, G or C
168 <400> SEQUENCE: 10
OK> 169 ggccnnnnng gcc
172 <210> SEQ ID NO: 11
173 <211> LENGTH: 13
174 <212> TYPE: DNA
175 <213> ORGANISM: Artificial
177 <220> FEATURE:
178 <223> OTHER INFORMATION: Artificial DNA
181 <220> FEATURE:
182 <221> NAME/KEY: misc_feature
183 <222> LOCATION: (5)..(9)
184 <223> OTHER INFORMATION: n = nucleotide A, T, G or C
OK> 186 <400> SEQUENCE: 11
187 ccggnnnnncc cgg
190 <210> SEQ ID NO: 12
191 <211> LENGTH: 5
192 <212> TYPE: DNA
193 <213> ORGANISM: Artificial
195 <220> FEATURE:
196 <223> OTHER INFORMATION: Artificial DNA
198 <400> SEQUENCE: 12
199 aggcc
202 <210> SEQ ID NO: 13
203 <211> LENGTH: 5
204 <212> TYPE: DNA
205 <213> ORGANISM: Artificial
207 <220> FEATURE:
208 <223> OTHER INFORMATION: Artificial DNA
210 <400> SEQUENCE: 13
211 ccggg
214 <210> SEQ ID NO: 14
215 <211> LENGTH: 46

21

13

13

5

5

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216-221 TYPE: DNA
217-221 ORGANISM: Artificial
219-220 SEQUENCE: 14
220-223 OTHER INFORMATION: Artificial DNA
222-400 SEQUENCE: 14
223 gaatggcca ttaaggctg caggatccgg caggatggg ctcgag

Please Note:
Use of ~~Grand/or~~ ~~Xaa~~ have been detected in the Sequence Listing. Please review the
sequences to ensure that corresponding explanation is presented in the ~~<220>~~
to ~~<223>~~ fields of each sequence which presents at least one n or Xaa.

Seq#:1; N Pos. 21,22,23,24
Seq#:3; N Pos. 21,22,23,24
Seq#:5; N Pos. 1,2,3,4
Seq#:7; N Pos. 1,2,3,4
Seq#:10; N Pos. 5,6,7,8,9
Seq#:11; N Pos. 5,6,7,8,9

Invalid <213> Response:

Use of "Artificial" only as "<213> Organism" response is incomplete,
per 1.823(b) of New Sequence Rules. Valid response is Artificial Sequence....

Seq#:1,2,3,4,5,6,7,8,9,10,11,12,13,14

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REPLACED CURRENT APPLICATION NUMBERS
L:9 M:290 C: Current Application Number differs, replaced current Application Number
L:10 M:271 C: Current Application Number differs, replaced current Application Number
L:37 M:341 W: (46) "n" or "Xaa" used, for SEQ ID# 3 after pos: 0
L:67 M:341 W: (46) "n" or "Xaa" used, for SEQ ID# 5 after pos: 0
L:97 M:341 W: (46) "n" or "Xaa" used, for SEQ ID# 7 after pos: 0
L:127 M:341 W: (46) "n" or "Xaa" used, for SEQ ID# 10 after pos: 0
L:169 M:341 W: (46) "n" or "Xaa" used, for SEQ ID# 11 after pos: 0
L:187 M:341 W: (46) "n" or "Xaa" used, for SEQ ID# 11 after pos: 0

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